3.A.1. Literature Studies: Two 6-month plaque/gingivitis clinical trial studies published in 1997 evaluated dentifrice formulations of 0.454% stannous fluoride in a silica base containing stannous chloride, polyphosphate, and citrate and reported statistically significant reductions in plaque mass and gingivitis.[48,49]

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[48] Mankodi, S. et. al.: Clinical Efficacy of an Optimized Stannous Fluoride Dentifrice, Part 2: A 6-Month Plaque/Gingivitis Clinical Study, Northeast USA, Compendium (Special Issue); 18: pp10-15, 1997.

[49] Williams C. et. al., Clinical Efficacy of an Optimized Stannous Fluoride Dentifrice, Part 3: A 6-Month Plaque/Gingivitis Clinical Study, Southeast USA, Compendium (Special Issue); 18: pp16-20, 1997.

3.A.1.1. "A 6-Month Plaque/Gingivitis Clinical Study, Northeast USA" (Appendix 3); "A 6-Month Plaque/Gingivitis Clinical Study, Southeast USA" (Appendix 4).

The two publications described identical protocols for 6-month, double blind clinical studies to investigate the efficacy of the stannous fluoride formulation for the control of supragingival dental plaque and gingivitis. The clinical trials and protocol were conducted following the American Dental Association guidelines and satisfy the clinical testing criteria recommended by the Subcommittee. The primary investigators for the Northeast and Southeast studies were Suru Mankodi, BDS, DDS, MSD (Perio) and Craig Williams, DDS, respectively. A total of 105-115 adult men and women took part in each study, and were randomly assigned to either a 0.454% stannous fluoride dentifrice or a control dentifrice containing 0.243 % sodium fluoride. After study group assignment, subjects were given a complete oral prophylaxis that included removal of all supragingival plaque and calculus deposits. Subjects were instructed to brush their teeth twice a day (morning and evening) for one minute. Subjects were evaluated for plaque and gingivitis after 3 and 6 months of use. Hard and soft tissues of the oral cavity were visually inspected for the presence of adverse reactions.

Results from both studies showed a statistically significant reduction in Plaque Index, Plaque Severity Index, Gingival Index, and Gingivitis Severity Index at 3 and 6 months of treatment with the stannous fluoride dentifrice. The 6-month clinical data are presented below.

Northeast USA Study
The Effect of 0.454% Stannous Fluoride Dentifrice on Plaque and Gingivitis

6 Months Treatment

Index	Control Dentifrice (n= 54) mean ± sd	0.454% Stannous Fluoride Dentifrice (n=50) mean ± sd	Percent Reduction (*vs.* Control)	Significance*
Plaque	2.610±0.530	2.080±0.410	20.3%	*P*<0.0001
Plaque Severity	0.547±0.255	0.242±0.201	55.8%	*P*<0.0040
Gingivitis	1.190±0.160	0.940±0.140	21.0%	*P*<0.0001
Gingivitis Severity	0.205±0.146	0.044±0.057	78.5%	*P*<0.0001

* Significance of comparison of baseline-adjusted (6-month) mean scores

Southeast USA Study
The Effect of 0.454% Stannous Fluoride Dentifrice on Plaque and Gingivitis

6 Months Treatment

Index	Control Dentifrice (n= 58) mean ± sd	0.454% Stannous Fluoride Dentifrice (n=54) mean ± sd	Percent Reduction (*vs.* Control)	Significance*
Plaque	2.200±0.460	1.700±0.400	22.7%	*P*<0.001
Plaque Severity	0.361±0.173	0.175±0.127	51.5%	*P*<0.001
Gingivitis	1.300±0.150	1.010±0.130	22.3%	*P*<0.001
Gingivitis Severity	0.319±0.139	0.082±0.093	74.3%	*P*<0.001

* Significance of comparison of baseline-adjusted (6-month) mean scores

No adverse effects on the oral hard or soft tissues were either observed or reported by the participants, including those who dropped out. At the 6-month examination in both studies, the magnitude of the percent reductions exceeded 20% for all four parameters: plaque index, plaque severity index, gingivitis index, and gingivitis

severity index. It is noteworthy that plaque mass reductions were statistically significant (>20%) in both studies and no tooth staining was reported. These antiplaque effects are consistent with the plaque mass reductions demonstrated by CPC and essential oils in studies previously filed to the call-for-data, and which the Subcommittee used as the basis for specifying the "antiplaque" statement of identity and indication for CPC and essential oils in the ANPR.